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CITATION:

INAMI, KENICHI. Effect of the Spleen on the Thyroid Gland (I) : Sudden Enlargement of the Thyroid Gland due to Catecholamin Administration in Patients with Splenomegaly. 日本外科宝函 1964, 33(5): 849-862

ISSUE DATE:

1964-09-01

URL:

http://hdl.handle.net/2433/205756

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Effect of the Spleen on the Thyroid Gland (I)

Sudden Enlargement of the Thyroid Gland due to Catecholamine Administration in Patients with Splenomegaly

by

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Received for Publication July 31, 1964

INTRODUCTION

There are several reports on the sudden temporary enlargement of the thyroid gland. This phenomenon is found most frequently in patients who are suffering from chromaffin cell tumors of the adrenal medulla when they are in hypertensive attacks. STRÖMBECK and HEDBERG[32] reported a case in 1939 : This case was a housewife, she had had all the symptoms and signs of paroxysmal hypertension. Her neck started to swell soon after the attacks had started, and stopped swelling as the attacks ceased and returned to normal. According to the measurement, the circumference of her neck was 35cm in between attacks and 39cm average during three attacks. This phenomenon is also observed in the patients who are in the early stage of GRAVE's disease : When these patients are in emotional excitement, they suddenly get expressions with the frightened stare and at the same time their thyroid glands are enlarged.

Similar sudden temporary enlarment of the thyroid gland was observed by the present author in two patients with splenomegaly, when they were injected noradrenaline (N. A.) subcutaneously for FREY's test ; and in these cases the enlargement subsided within half an hour. Furthermore, though this sudden temporary enlargement of the thyroid gland was observed every time when N. A. was injected before splenectomy, it was no longer observed after splenectomy in spite of the same injection of N. A., suggesting a correlation between the spleen and the thyroid gland. Discovery of these phenomena was the starting point of this research, in which the cause of the phenomena, and how they are related to splenomegaly, were investigated.

THE TWO CASES

CASE A. A woman, aged 22 years, had been suffering from hereditary hemolytic jaundice. Soon after the injection of 0.5cc of 1/1000 N. A. subcutaneously for FREY's test before splenectomy, a soft swelling appeared on the part of her thyroid gland. Her neck swelled up suggesting a goiter. She started complaining of a feeling of constriction in her throat about 5 minutes after the injection, and her thyroid gland was remark-

ably enlarged and its contours were clearly visible, and the overall gland was bulging. (Fig. 1, Fig. 2) The neck, which was 32.0cm in circumference before the injection, swelled and increased to 33.5cm in circumference 10 minutes after the injection (Fig. 3); and 30 minutes after the injection, the swelling of the thyroid gland disappeared and the neck returned to its normal state (Fig. 4). The measurement of cervical circumference, the pulse rate and the degree of palpitation are shown in Table 1. By the same N. A. injection, this phenomenon was observed repeatedly, until she was splenectomized for the treatment of jaundice. The spleen taken out weighed 550g, and in its histological investigation, marked hyperplasia of venous sinus, congestion of reticular system and slight hemosiderosis were observed. The most interesting point with this case was that two weeks after the operation, this patient had another injection of N. A., exactly in the same manner and dosage as the ones preceding the operation, no enlargement of the thyroid gland was observed.

Table 1 cervical circumference of CASE A after injection of N. A.

I before operation

	pulse rate	palpitation	cervical c.
before	72/min.	(−)	32.0cm
5 min.	60	(+)	33.0
10	60	(+)	33.5
15	56	(−)	33.5
20	64	(−)	33.5
25	68	(−)	32.5
30	72	(−)	32.0

II after operation

	pulse rate	palpitation	cervical c.
before	76/min.	(−)	30.5cm
5 min.	56	(+)	30.5
10	56	(+)	31.0
15	60	(−)	30.5
20	60	(−)	30.5

Table 2 cervical circumference of CASE B after injection of N. A.

I before operation

	cervical c.
before	28.5cm
5 min.	30.0
10	30.2
15	29.8
20	29.5
25	29.0
30	28.5
60	28.5

II after operation

	blood pressure	palpitation	cervical c.
before	100/68mmHg	(−)	28.0cm
5 min.		(+)	28.2
10	168/90	(+)	28.3
15		(+)	28.3
20		(−)	28.3
25		(−)	28.1
30		(−)	28.0
60	98/64	(−)	28.0

CASE B. Another case was a housewife, aged 58 years, suffering from BANTI's syndrome. Just like in CASE A, she was injected 0.5cc of N. A. subcutaneously for FREY's test before splenectomy. Several minutes after, a soft swelling started to appear on her neck, and the contours of her thyroid gland were clearly visible. Her neck was 28.5cm in circumference before the injection, and 10 minutes after the injection it became 30.2cm, and at the same time remarkable distension of the neck veins was observed. Within half an hour, the swelling subsided and her neck resumed its normal circumference (Table 2). She was splenectomized for the treatment of anemia. The spleen taken out weighed 545g, and in its histological investigation, fibroadenia of red pulp, remarkable thickening of capsule and

trabecula, and atrophy of lymph follicles were observed. Two weeks after splenectomy, she was injected the same amount of N. A., but the enlargement of the thyroid gland was not observed.

CLINICAL INVESTIGATION

For further researches about this phenomenon of sudden enlargement of the thyroid gland, 13 patients with splenomegaly and 12 control patients without splenomegaly were investigated. They were injected N. A. both before and after their respective operations, to find out if there were any differences between the patients with and without splenomegaly concerning the reaction of the thyroid gland to N. A., as well as how it changed after splenectomy. Moreover, their thyroid glands taken by means of biopsy were investigated to know if any histological changes of the thyroid gland were caused by splenomegaly.

The 13 patients with splenomegaly were, 10 cases of BANTI'S syndrome, 2 cases of hereditary hemolytic jaundice and one case of acquired hemolytic jaundice. All of the 13 cases were splenectomized for treatment ; and both before and after their operations, 0.5cc of 1/1000 N. A. was injected subcutaneously to investigate the swelling of the neck. At the same time, histological investigation was made on the thyroid glands taken by means of biopsy on 8 out of the 13 cases.

Table 3 increase of cervical circumference in patients with splenomegaly after injection of N. A. (before and after splenectomy)

	age	sex	diag.	cerv. c.	portal p.	spleen	spleen	thyroid gland
CASE A	22	f	h.h.j.	1.5—0.5cm	180—210mmH_2O	550g	hyperplasia of sinus, congested reticulum	
CASE B	58	f	B.	1.7—0.3	270—200	545	fibroadenia	
CASE 1	20	f	h.h.j.	1.0—0.3	130—128	380	congested reticulum, G-G body	
CASE 2	31	m	h.j.	0.5—0.5	200—160	480		
CASE 3	27	m	B.	1.0—1.0	430—358	960	fibroadenia, periarterial fibrosis	
CASE 4	59	f	B.	0.7—0.5	240—180	1,200	fibrosis of reticulum, hemosiderosis	
CASE 5	25	m	B.	0.7—0.5	220—180	520	fibroadenia	slightly congested
CASE 6	57	f	B.	1.0—0.4	320—260	800	fibroadenia	markedly congested interstitial hyperplasia
CASE 7	23	m	B.	0.6—0.4	220—200	540	marked fibroadenia	
CASE 8	44	f	B.	1.5—0.6	256—245	1,200	scarce fibrosis, hyperplasia of sinus	moderately congested
CASE 9	24	m	h.h.j.	0.6	225—215	715	congested riticulum	moderately congested
CASE 10	37	m	B.	0.5—0.5	300—240	810	fibroadenia	slightly congested, atrophy of gland
CASE 11	33	f	B.	0.8—0.4	240—210	480	fibroadenia	markedly congested
CASE 12	42	f	B.	0.5—0.5	112—100	745	scarce fibrosis, hyperplasia of sinus	markedly congested
CASE 13	33	f	B.	1.0—0.6	410—350	1,040	fibroadenia	markedly congested

h. h. j. : hereditary hemolytic jaundice B. : BANTI's syndrome h. j. : hemolytic jaundice

Out of the 12 control patients without splenomegaly, 7 cases were injected 0.5cc of 1/1000 N. A., both before and after their respective operations, for the investigation of the swelling of the neck ; and the other 5 cases were biopsied of their thyroid glands for histological investigation.

THE 13 CASES WITH SPLENOMEGALY Their ages, sexes, diagnoses, increases in cervical circumference by the injection of N. A. both before and after splenectomy, portal pressures before and after splenectomy, weights of the removed spleens, etc., are shown in Table 3.

CASE 1. (20yr. female) By the injection of N. A., a soft swelling in the region of the thyroid gland was induced before the operation. Her neck was 31.0cm in circumference before the injection, and 10 minutes after the injection it became 32.0 cm, and returned to its normal state in 20 minutes. Three weeks after splenectomy, the swelling of the neck was no longer induced by the injection of N. A. (Table 4).

Table 4 cervical circumference of CASE 1 after injection of N. A.

I before operation

	blood pressure	pulse rate	resp.	palp.	cervical c.
before	106/86mmHg	80/min.	26/min.	(−)	31.0cm
5 min.	114/90	60	22	(−)	31.0
10	152/76	66	24	(−)	32.0
15	120/60	68	24	(−)	31.5
20	120/60	75	26	(−)	31.0
25	118/60	80	24	(−)	31.0
30	114/66	80	28	(−)	31.0

II after operation

	blood pressure	pulse rate	resp.	palp.	cervical c.
before	106/56mmHg	68/min.	28/min.	(−)	30.5cm
5 min.	151/94	60	36	(+)	30.8
10	150/90	64	28	(−)	30.8
15	130/80	64	24	(−)	30.7
20	118/82	68	28	(−)	30.5
25	116/80	80	28	(−)	30.5
30	114/74	76	28	(−)	30.5

resp. : respiration palp. : palpitation

CASE 2. (31yr. male) The swelling of the neck by the injection of N. A. was not observed, either before or after splenectomy.

CASE 3. (27yr. male) Remarkable swelling on the neck was observed when N. A. was injected before splenectomy. He complained of a feeling of constriction in his throat ; his neck, 35.5cm in circumference before the injection, became 36.5cm 10 minutes after the injection, contours of the thyroid gland being clearly visible ; and the neck returned to its normal state in 25 minutes. The reaction of the thyroid gland to N. A., 12 days after the operation, was just the same as before the operation with remarkable swelling

Table 5 cervical circumferenc of CASE 3 after injection of N. A.

I before operation

	blood pressure	pulse rate	resp.	palp.	cervical c.
before	100/54mmHg	64/min.	24/min.	(−)	35.5cm
5 min.	100/74	56	36	(−)	36.0
10	138/84	42	36	(++)	36.5
15	132/94	45	36	(++)	36.4
20	128/90	54	30	(−)	35.8
25	122/82	60	27	(−)	35.5
30	122/76	60	24	(−)	35.5

II after operation

	blood pressure	pulse rate	resp.	palp.	cervical c.
before	125/72mmHg	92/min.	27/min.	(−)	35.5cm
5 min.	165/103	65	30	(++)	36.5
10	170/103	70	26	(+)	36.2
15	160/95	86	25	(−)	36.0
20	146/79	89	25	(−)	35.5
25	142/75	90	26	(−)	35.5
30	123/70	93	27	(−)	35.5

on the neck (Table. 5).

CASE 4. (59yr. female) The swelling of the neck due to N. A. was not observed, either before or after splenectomy.

CASE 5. (25yr. male) By the injection of N. A., his neck increased in circumference by 0.7cm before the operation, and 0.5cm after the operation, but the swelling of the thyroid gland was not observed. Histological investigation of his thyroid gland was made by means of biopsy : Follicles were normal in size, follicle epithelia were squamous, interstitium was slightly hyperplastic, and interfollicular capillaries were slightly congested ; the gland seemed to be normal in function.

CASE 6. (57yr. female) Before splenectomy, her neck on the thyroid gland swelled by the injection of N. A., and her cervical circumference increased by 1.0cm ; but the swelling was not observed after splenectomy. In the thyroid gland, follicles were normal and uniform in size, follicle epithelia were squamous, interstitium was hyperplastic ; and remarkable congestion of interfollicular capillaries was observed ; the gland seemed to be normal in function.

CASE 7. (23yr. male) The swelling of the thyroid gland was not observed, either before or after splenectomy.

CASE 8. (44yr. female) By the injection of N. A. before the operation, a soft swelling on the part of the thyroid gland appeared with a feeling of constriction in her throat. The neck, which was 36.0cm in circumference before the injection, became 37.5cm 5 minutes after the injection, and returned to its normal state in 20 minutes (Table 6). The swelling of the thyroid gland was no longer induced after splenectomy. In her thyroid gland, follicles with normal and uniform size, squamous follicle epithelia and

Table 6 cervical circumference of CASE 8 after injection of N. A.

I before operation

	blood pressure	pulse rate	resp.	palp.	cervicical c.
before	154/80mmHg	60/min.	24/min.	(−)	36.0cm
3 min.					37.0
5	184/94	56	24	(卄)	37.5
8					37.0
10	180/80	68	28	(卄)	36.5
15	150/70	64	24	(−)	36.5
20	150/74	76	20	(−)	36.0
25	150/74	76	20	(−)	36.0
30	136/76	84	24	(−)	36.0

II after operation

	blood pressure	pulse rate	resp.	palp.	cervical c.
before	146/82mmHg	64/min.	20/min.	(−)	35.5cm
5 min.	170/92	58	24	(卄)	36.0
10	170/90	62	24	(+)	36.1
15	154/76	68	22	(−)	35.8
20	148/70	68	22	(−)	35.8
25		72			35.6
30	140/72	66	22	(−)	35.6

remarkably congested interfollicular capillaries were observed (Fig. 5); the function of the gland seemed to be normal.

CASE 9. (24yr. male) The swelling of the neck due to N. A. was not observed. In his thyroid gland, slight congestion of inerfollicular capillaries was observed.

CASE 10. (37yr. male) The swelling of the neck was not observed. In his thyroid gland, interfollicular capillaries were slightly congested.

CASE 11. (33yr. female) The swelling of the neck was not observed. In her thyroid gland, interfollicular capillaries were remarkably congested.

CASE 12. (42yr. female) The swelling of the neck was not observed. Remarkable congestion of interfollicular capillaries was observed in her thyroid gland.

CASE 13. (33yr. female) By the injection of N. A., a soft swelling on the part of the thyroid gland was induced before splenectomy. Her neck, which was 33.0cm in circumference before the injection, became 34.0 cm 10 minutes after the injection, and returned to its normal state in 30 minutes. The swelling was no longer induced after splenectomy. In her thyroid gland: Follicles were normal and uniform in size, and full of colloid ; follicle epithelia were squamous and not hyperplastic. Remarkable congestion of interfollicular capillaries (Fig. 6) and slight interstitial hyperplasia were observed.

THE 12 CONTROL CASES WITHOUT SPLENOMEGALY Their ages, sexes and diagnoses are shown in Table 7 and Table 8.

CASE 101 to 107. They were injected 0.5cc of 1/1000 N. A. both before and after their respective operations, but in none of them the swelling of the thyroid gland was

Table 7 control : increase of cervical circumference in patients without splenomegaly after injection of N. A. (before and after operation)

	age	sex	cerv. c.	diagnosis
CASE 101	62	f	0.3—0.4cm	cholelithiasis
CASE 102	20	f	0.5—0.5	diagnostic laparotomy
CASE 103	18	m	0.3—0.5	appendicitis chronica
CASE 104	58	f	0.3—0.3	mammary cancer
CASE 105	61	m	0.2—0.2	gastric cancer
CASE 106	31	m	0.4	hemorrhoids
CASE 107	55	f	0.5—0.4	cholecystitis

Table 8 control : thyroid gland in patients without splenomegaly

	age	sex	diagnosis	thyroid gland
CASE 201	27	f	lung tuberculosis	not congested
CASE 202	37	m	lung tuberculosis	not congested
CASE 203	27	m	lung tuberculosis	interstitial hyperplasia, not congested
CASE 204	20	f	diagnostic laparotomy	not congested
CASE 205	63	m	lingual cancer	interstitial hyperplasia, not congested

observed ; the increases in cervical circumference due to N. A. were less than 0.5cm in all cases, and the neck returned to normal state within 20 to 30 minutes after the injection. There was no difference between the pre- and postoperative increases (Table 7).

CASE 201 to 205. Their thyroid glands were taken by means of biopsy: In all cases, follicles were normal and uniform in size, and full of colloid ; follicle epithelia were squamous, and not hyperplastic ; the glands seemed normal in function. Congestion of the interfollicular capillaries or cell infiltration were not found (Fig. 7) ; moderate interstitial hyperplasia was observed in two cases.

EXPERIMENTAL INVESTIGATION

To make further investigation of effects on the histology of the thyroid gland of the swelled spleen, the thyroid glands of rabbits with experimental splenomegaly were studied histologically.

EXPERIMENTAL PROCEDURE Normal, young, white rabbits weighing about 2.0 kilograms, were used throughout the experiment. Rabbits were divided into 4 groups (Group-I, II, III, IV).

In Group-I, experimental splenomegaly was produced. For the production of experimental splenomegaly, albumin sensitization method (SUZUKI) was used : 2cc per kg of bodyweight of 1% albumin in physiologic saline solution was intravenously injected to 30 rabbits, daily for 3 months. The spleens were swelled in all cases, and weighed 2.10 to 6.65g, while the spleens of control animals weighed less than 1.0g (Fig. 8).

The swelled spleens were histologically investigated : Atrophy of lymphfollicles, thickening of capsule and trabecula, hyperplasia of reticulum cells and reticulum fibers, hyperplasia and gland-like structure of venous sinus, and periarterial fibrosis were observed ;

these findings resemble to those in BANTI'S syndrome. Cell infiltration in red pulp chiefly consisting of plasma cells and/or eosinophil leukocytes was observed in some cases. Remarkable hemosiderosis, congestion in red pulp were observed in some other cases ; these findings resemble to those in hemolytic jaundice.

Group-II was normal control group, consisting of 10 normal rabbits. In Group-III, as control experiment, 5 rabbits were splenectomized ; and 30 days after the operation, their thyroid glands were investigated. In Group-IV, as another control experiment, 9 rabbits were splenectomized first ; and 30 days after the operation, they were sensitized with albumin for 3 months just as Group-I.

RESULTS The thyroid glands of rabbits of each groups were investigated histologically.

Group-I (experimental splenomegaly, produced by albumin sensitization) : In most cases, follicles were normal in size, but small in some cases. Follicle epithelia were mostly squamous, but cuboidal in some cases, and slight hyperplasia of follicle epithelia were observed in some other cases. Interfollicular capillaries were remarkably congested in all cases (Fig. 9, Fig. 10). Interstitial hyperplasia and cell infiltration were not found. The glands seemed normal in function.

Group-II (normal control) (Fig. 11), Group-III (30 days after splenectomy) (Fig. 12) and Group-IV (albumin sensitization after splenectomy) (Fig. 13) : Follicles were normal and uniform in size, and full of colloid. Follicle epithelia were squamous, and not hyperplastic. Congestion of interfollicular capillaries, interstitial hyperplasia or cell infiltration were not observed. The glands seemed normal in function. Interstitial congestion was observed in some cases in Group-III.

CONSIDERATION

In the clinical investigation, in 5 out of the 13 patients with splenomegaly, the swelling in the region of the thyroid gland was observed by the injection of N. A. ; and the swelling was no longer observed after splenectomy in 4 out of the 5 cases in spite of the same injection of N. A. In Case 3, the enlargement of the thyroid gland due to N. A. was observed after splenectomy just as before ; but this might be due to the fact that postoperative N. A. was given too early after the operation in this case (only 12 days after splenectomy). On the other hand, in 7 control patients without splenomegaly, the swelling of the neck was not observed at all by the injection of N. A., either before or after their respective operations. The increases in cervical circumference by the injection of N. A. in 7 control patients were less than 0.5cm, averaging 0.37cm, both before and after their operations. In 13 patients with splenomegaly, however, even in the cases in whom the swelling of the neck was not observed, the increases in cervical circumference by the injection of N. A. before splenectomy were larger than 0.5cm ; and after splenectomy, the increases reduced and became almost equal to the control average, except for one case. This phenomenon suggests that the swelled spleen has an effect on the reaction of the thyroid gland to N. A.

No correlation was found between the degree of the swelling of the neck and portal pressure, weight of the spleen, histological findings of the spleen, etc. The swelling of

the neck was observed both in BANTI's syndrome and hemolytic jaundice (Table 3).

The thyroid glands of the patients with splenomegaly were investigated histologically : Size of follicles, form of follicle epithelia, nature of colloid, etc., were normal ; and hyperplasia of follicle epithelium or interstitium, cell infiltration were scarcely observed. Congestion of interfollicular capillaries was observed in all cases ; and this was observed in none of the control patients. No correlation, however, was found between the degree of congestion and the degree of swelling of the neck (Table 3).

This fact, interfollicular congestion of the thyroid gland in case of splenomegaly, was reassured by experimental investigation on rabbits : In the thyroid glands of rabbits with experimental splenomegaly (produced by albumin sensitization), marked interfollicular congestion was observed ; while no congestion was observed in the thyroid glands of not only normal but those rabbits sensitized with albumin after splenectomy. These facts suggest an correlation between the swelled spleen and the congestion in the thyroid gland.

BELT[3] reported a case in which the interfollicular capillaries of the thyroid gland of a patient suffering from pheochromocytoma, whose neck swelled during hypertensive attacks, were congested but the gland was normal in size. Congestion of interfollicular capillaries of the thyroid gland, therefore, might be related with the sudden enlargement of the thyroid gland.

There are a few reports on the histological changes of the thyroid gland in BANTI's disease : FUKUJI (1931)[8] reported that there was no recognizable changes. According to TAKEUCHI (1950)[35], however, the gland was hypo- or dysfunctional, and remarkable congestion was observed.

The histological changes caused by splenectomy were also studied by several investigators : IZUMI (1924)[17] reported that a week after splenectomy, capillaries in the thyroid gland were congested in dogs, due to decreased reactivity to adrenaline caused by the removal of the spleen. NISHIMURA (1928)[24] reported that hypofunction of the thyroid gland was observed 1 to 7 months after splenectomy in white rat. SUMORI and INOUE (1932), FUJIKAWA[6] (1936), and FUJIMURA (1955)[7] reported that hyperfunction of the thyroid gland was observed until 30 days after splenectomy, and then hypofunction of it. These facts, too, suggest an effect of the spleen on the thyroid gland.

There are several reports on sudden temporary enlargement of the thyroid gland. STRÖMBECK and HEDBERG[32] described a case in 1939, as mentioned in the introduction. HOWARD and BARKER reported 2 cases of pheochromocytoma in 1937, whose neck swelled greatly, suggesting a goiter, during paroxysms of hypertension. BAUER and BELT[2] reported in 1947 on a housewife of pheochromocytoma, whose attacks of hypertension were associated with the swelling of the neck. During an attack her thyroid gland was remarkably enlarged, and its contours were clearly visible. Swelling of the neck coinciding with the attacks of hypertension in cases of pheochromocytoma was also described by those people as follows : BELT and POWELL[3], BURGESS et al.[22], VAN EPPS et al.[22] and MAYOCK and ROSE.[22] CANNON[22] reported in 1929, sudden enlargement of the thyroid gland of a woman, who was in the early stage of GRAVE's disease. In a great emotional excitement, she had at once a sense of constriction in her throat and was troubled with difficulty in swallowing, and the thyroid gland enlarged ; six weeks after the incident, she had B.M.R. 65% above the normal.

Since these enlargement of the thyroid gland, including those observed in splenomegalic patients in case of N. A. injection, are sudden and temporary, this phenomenon is considered to be due to changes in blood flow in the thyroid gland. Enlargement of the thyroid gland observed in pheochromocytoma is naturally due to catecholamine (C. A.) secreted from the tumor. In GRAVE's disease, emotional excitement leads to overaction of adrenal medulla and outpouring of excessive amount of C. A., and enlargement of the thyroid gland is considered to be due to this C. A. Therefore, these sudden enlargements of the thyroid gland are caused by changes in thyroidal blood flow due to C. A.

It is reported that the thyroid gland is supplied with the greatest blood flow per unit weight in all mammalian tissues (SHINABERGER[29]), and is the most sensitive in the body in its reaction to C. A. (GUNNING[10]) ; and there are many reports on the changes in thyroidal blood flow due to C. A. GUNNING (1917)[10] investigated thyroidal blood flow with the venous outflow technique, and concluded that epinephrine caused marked diminution in blood flow followed by some increase as an after effect. SCHKAWERA (1925), SHINABERGER (1956)[29], SÖDERBERG (1958)[30] and many others reported the similar effect.

But there is another kind of reports on the reactions of thyroidal blood flow to C. A. MASON[21] studied plethysmography of the thyroid gland in dogs, and reported that in about a fourth of the experimented cases, injection of 0.1 to 0.2mg of epinephrine was followed by definite increase in volume of the thyroid gland. ENGEL (1926)[4] reported that, when solution of 1/1000 epinephrine was applied locally to one lobe of the the thyroid, while the opposite lobe was used as a control, there was marked congestion of the portion to which it was applied. He also reported that following the intravenous injection of 4mg of epinephrine to a dog, there was marked bilateral engorgement, which persisted for about five minutes, then the gland shrank. According to BARNETT et at. (1950)[1], in two subjects receiving 30 microgrammes of N. A. per minute for 16 and 40 minutes respectively, a soft swelling in the region of the thyroid gland developed. In the subject receiving the shorter infusion, the swelling subsided within an hour, and in the other, at the end of the infusion, the neck measured 44cm in circumference and after 6 hours resumed the normal measurement of 39cm. MENOF (1954)[22] reported that, in a subject, receiving 24 microgrammes per minute of N. A. for ten minutes, the neck increased by 3cm in circumference due to enlargement of the thyroid gland. According to these reports, a large amount of C. A. is considered to increase thyroidal blood volume.

The fact that the hypertensive attacks of pheochromocytoma, accompanied by sudden enlargement of the thyroid gland, are caused by a large amount of C. A., was demonstrated by STRÖMBECK et al. : They investigated blood pressure and blood sugar of a house wife of pheochromocytoma, during her hypertensive attacks accompanied by the swelling of the thyroid gland ; they investigated also her blood pressure and blood sugar after injection of various amount of epinephrine ; and found that 2mg of epinephrine corresponded best with the spontaneous attacks.

Concerning the sudden enlargement of the thyroid gland observed in patients with splenomegaly in case of N. A. injection, it may be considered that thyroidal reaction which is to be caused by a large amount of C.A. in normal case, is caused by relatively small amount of C. A., due to the fact that reactivity of the thyroid gland to C. A. is changed

by the swelled spleen.

VON EULER[5] proved that the spleen contains a large amount of C. A. next to adrenal medulla, and MORI demonstrated histochemically an abundant chromaffin substance in the spleens of splenomegalic patients and rabbits with experimental splenomegaly. There is a possibility that C. A. in the swelled spleen is outpoured into general circulation when the spleen contracts by the injection of N. A. But in view of various clinical data, such as blood pressure, it is doubtful that such a large amount of C. A. as secreted from pheochrocytoma, be mobilized from the swelled spleen on the occasion of its contraction.

SUMMARY

1. Sudden temporary enlargement of the thyroid gland was observed in some patients with splenomegaly after the injection of N. A. This sudden enlargement of the thyroid gland was no longer observed after splenectomy, in spite of the same injection of N. A.
2. The thyroid glands of patients with splenomegaly were histologically investigated by means of biopsy : Functions seemed normal ; but interfollicular capillaries were congested in all cases.
3. Interfollicular capillaries in the thyroid glands of rabbits with experimental splenomegaly (produced by albumin sensitization) were congested remarkably in all cases ; whereas no congestion was observed in the thyroid glands of normal rabbits and rabbits sensitized with albumin after splenectomy.
4. These facts suggest an effect of the spleen in pathological conditions on the thyroid gland.

The author's grateful thanks are given to Professor Dr. C. KIMURA, for his helpful suggestions in the course of the work. The author also wishes to express his sincere gratitude to Drs. K. TSUNEKAWA, T. KUYAMA, M. OKAMOTO, H. HIGASHINO, K. MORI for their cooperation. The gist of the present study was reported by Professor Dr. C. KIMURA at the 33rd General Congress of the Japan Endocrinological Society (April, 1960), and International Catecholamine Confernce (May, 1960) ; and by the author at the 3rd General Cogrress of the Japan Clinical Neurological Society (April, 1962.)

BIBLIOGAPHY

1) Barnett, A. J., Blacket, R. B., Depoorter, A. E., Sanderson, P. H. & Wilson, G. M. : The action of noradrenaline in man and its relation to pheochromocytoma and hypertension. Clin. Sci., **9**, 151, 1950.
2) Bauer, J. & Belt, E. : Paroxysmal hypertension with concomitant swelling of the thyroid due to pheochromocytoma of the right adrenal gland. Cure by surgical removal of the pheochromocytoma. J. Clin. Endocr., **7**, 30, 1947.
3) Belt, A. E. & Powell, T. O. : Clinical manifestations of the chromaffin cell tumors arising from the suprarenal medulla. Surg. Gynec. Obstet., **59**, 9, 1934.
4) Engel, A. & Euler, U. S. V. : Diagnostic value of increased urinary output of noradrenaline and adrenaline in pheochromocytoma. Lancet, **259**, 387, 1950.
5) Euler, U. S. v. : Noradrenaline. Charles C Thomas Publisher, Springfield, Illinois, 1956.
6) Fujikawa, T. : Wechselbeziehung zwischen der Schilddrüse und der Milz. (5) Histologische Untersuchung. (in Japanese) Okayama Igakkai Z., **48**, 1531, 1936.
7) Fujimura, A. : The effects of splenectomy on the functions of the thyroid and parathyroid glands. (in Japanese) Folia Endocr. Jap., **31**, 459, 1955.
8) Fukuji, S. : Beiträge zur so-genannte Bantische Krankheit. (7), (8), (9) and (10). Grenzgebiet (Tokyo), **5**, 369 and 506 and 639 and 789, 1931.
9) Goldenberg, M. : Adrenal medullary function. Amer. J. Med., **10**, 627, 1951.

10) Gunning, R. E. L. : The effects of adrenin on the distribution of the blood. Amer. J. Physiol., **44**, 215, 1917.
11) Hanatani, J. : A study on the mechanism of an increase in portal pressure in portal hypertension. (in Japanese) J. Osaka City Med. Cent., **7**, 687, 1958.
12) Holton, P. : Noradrenaline in adrenal medullary tumours. Nature, **163**, 217, 1949.
13) Homma, H., Ishii, J., Saito, T., Ishimi, Z., Kuzuya, N., Asai, T., Ishiwatari, K., Yoshiue, S., Fukuoka, T., O, oto, S., Takeuchi, K., Nishimura, M., Shimamine, T., Matsushita, R. and Inoue, N. : A case of pheochromocytoma. (in Japanese) Saishin Igaku, **15**, 150, 1960.
14) Imaizumi, R. : Quantification of catecholamines. (in Japanese) Saishin Igaku, **15**, 16, 1960.
15) Imanaga, H. : Diagnosis and treatment of portal hypertension.(in Japanese) J. Jap. Surg. Soc., **57**, 1014, 1957.
16) Ito, S. : Experimental hemolytic anemia. J. Osaka City Med. Cent., **6**, 938, 1957.
17) Izumi, G. : The effect of splenectomy on the liver. (in Japanese) J. Jap. Surg. Soc., **25**, 1201, 1924.
18) Kimura, C. : Surgical significance of catecholamine. (in Japanese) Saishin Igaku, **15**, 68, 1960.
19) Kimura, C., Sugitani, A., Yamamoto, T. & Yura, R. : Several problems on catecholamines. (in Japanese) Saishin Igaku, **15**, 143, 1960.
20) Lund, A. : Adrenaline and noradrenaline in blood and urine in cases of pheochromocytoma. Scand. J. Clin. Lab. Invest., **4**, 263, 1962.
21) Mason, J. B., Markowitz, J. & Mann, F. C. : A plethysmographic study of the thyroid gland of the dog. Amer. J. Physiol., **94**, 125, 1930.
22) Menof, P. : Sudden enlargement of thyroid gland. Lancet, **267**, 996, 1954.
23) Mills, L. C. & Moyer, J. H. : The effects of various catecholamines on specific vascular hemodynamics in hypotensive and normotensive subjects. Amer. J. Cardiol., **5**, 652, 1960.
24) Nishimura, S. : Über Veränderungen der Drüsen mit innere Sekretion bei entmilzten Tieren. (in Japanese) Folia Endocr. Jap., **4**, 1905, 1928.
25) Okinaka, S., Sano, I., Kimura, C., Yoshiue, S., Yoshikawa, M. & Asano, S. : On catecholamines. (in Japanese) Saishin Igaku, **15**, 94, 1960.
26) Palmer, J. G., Eichwald, E. J., Cartwright, G. E. & Wintrobe, M. M. : The experimental production of splenomegaly, anemia and leukopenia in albino rats. Blood, **8**, 72, 1953.
27) Redisch, W., Crinis, K. D. & Steele, J. M. : Studies on vasoactivity of catecholamines in man. Amer. J. Cardiol., **5**, 660, 1960.
28) Sarnoff, S. J. : Certain aspects of the role of catecholamines in circulatory regulation. Amer. J. Cardiol., **5**, 579, 1960.
29) Shinaberger, J. H. & Bruner, H. D. : Blood flow in the thyroid gland of the dog. Fed. Proc., **15**, 483, 1956.
30) Söderberg, U. : Temporal characteristics of thyroid gland. Physiol. Rev., **39**, 777, 1959.
31) Streicher, H. J. : Pathophysiologische Grundlage der Splenektomie. Langenbeck Arch. Klin. Chir., **289**, 614, 1958.
32) Strömbeck, J. P. & Hedberg, T. P. : Tumor of the suprarenal medulla associated with paroxysmal hypertension. Acta Chir. Scand., **82**, 177, 1939.
33) Sugitani, A. : The experimental study on the concentration of plasma catecholamine in various states by Weil-Malherbe and Bone's method. Arch. Jap. Chir., **28**, 3793, 1959.
34) Suzuki, T. : Etiology and pathology of portal hypertension. (in Japanese) J. Jap. Surg. Soc., **57**, 987, 1957.
35) Takeuchi, H. : Histological changes of the thyroid in so-called Banti's disease. (in Japanese) Acta Med. (Fukuoka), **20**, 952, 1950.
36) Takemoto, I. : Histological changes of the submandibular and parotid glands caused by extirpation of the spleen. (in Japanese) Okayama Igakkai Z., **47**, 1866, 1935.
37) Tasaka, S. : Clinical significance of catecholamine. (in Japanese) Saishin Igaku, **15**, 60, 1960.
38) Thompson, W. P. : The pathogenesis of Banti's disase. Ann. Intern. Med., **14**, 255, 1941.
39) Tomoda, M. : Pathogenesis and pathology of portal hypertension.(in Japanese) J. Jap. Surg. Soc., **57**, 974, 1957.
40) Watts, C. F. : Changes in iodine content of the thyroid gland following changes in the blood flow through the gland. Amer. J. Physiol., **38**, 356, 1915.
41) Yamada, S. : Study on the etiology of the Banti's disease. (1) and (2). (in Japanese) J. Jap. Surg. Soc., **55**, 1201 and 1211, 1955.
42) Yamaguchi, Y. : The spleen and the endocrine glands. (in Japanese) Clin. Endocr. (Tokyo), **9**, 617, 1956.
43) Yamanaka, H. : A histopathological study of rabbit's spleen sensitized with egg white. (in Japanese) J. Osaka City Med. Cent., **6**, 530, 1957.

Fig. 1 CASE A. before the injection of N. A.

Fig. 2 CASE A. 5 minutes after the injcetion of N. A.

Fig. 3 CASE A. 10 minutes after the injection of N. A.

Fig. 4 CASE A. 30 minutes after the injection of N. A.

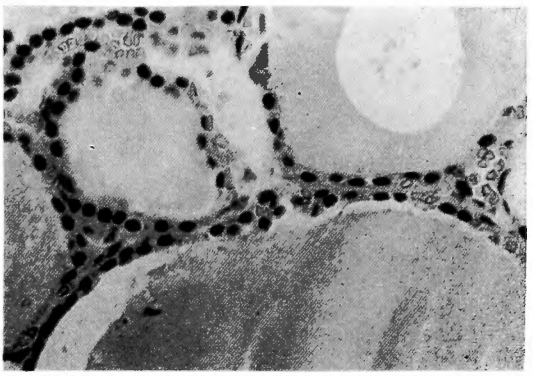

Fig. 5 thyroid gland (CASE 8). remarkable congestion of interfollicular capillaries (×400)

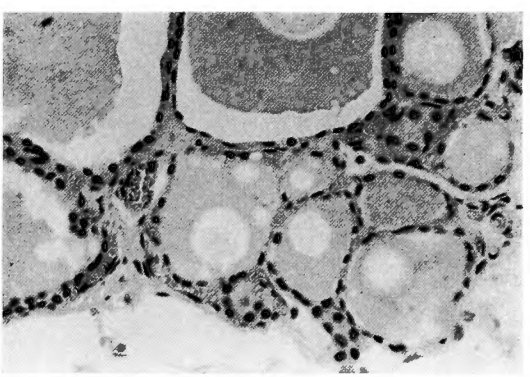

Fig. 6 thyroid gland (CASE 13). slight interstitial hyperplasia remarkable congestion of interfollicular capillaries (×280)

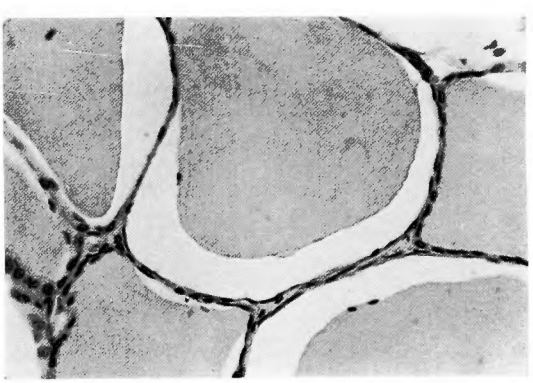

Fig. 7 thyroid gland (CASE 204). control (×280)

Fig. 8
2.35g 1.15g 2.10g 6.65g 2.75g 0.65g 1.00g spleens of albumin-sensitized rabbits (left) spleens of control rabbits (right)

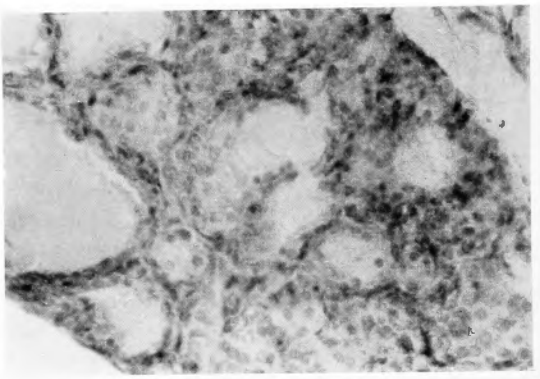

Fig. 9 thyroid gland (albumin-sensitized rabbit) remarkable congestion of interfollicular capillaries (×280)

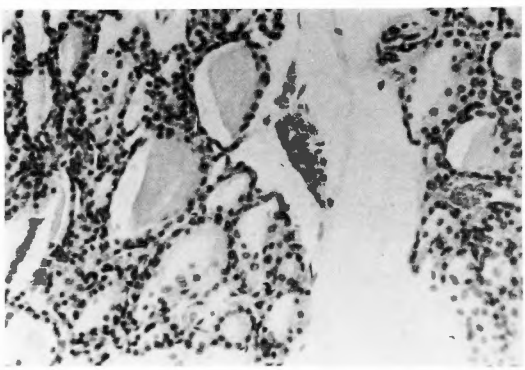

Fig. 10 thyroid gland (albumin-sensitized rabbit) remarkable congestion of interfollicular capillaries (×280)

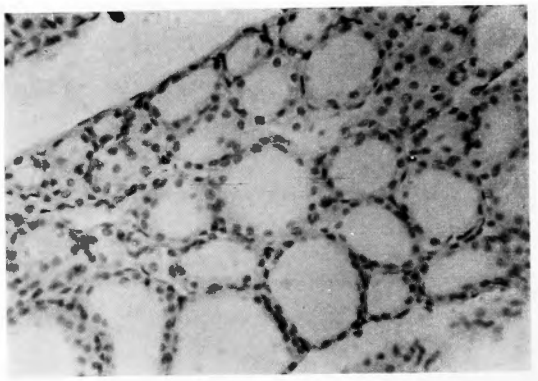

Fig. 11 thyroid gland (control rabbit). (×280)

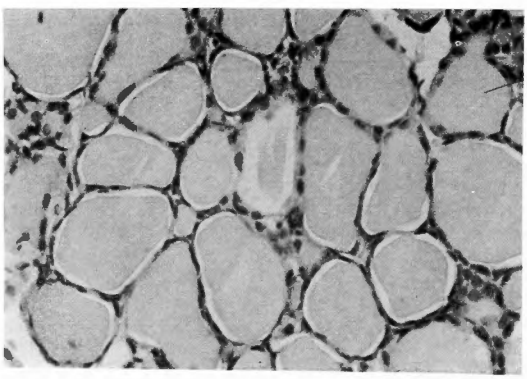

Fig. 12 thyroid gland (splenectomized rabbit) control (×280)

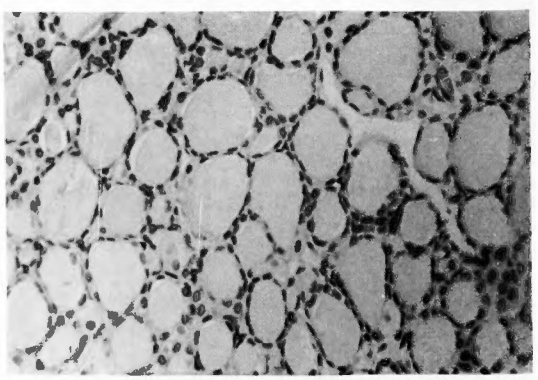

Fig. 13 thyroid gland (albumin-sensitized after splenectomy). control (×280)

和文抄録

脾臓と甲状腺の相互関係に関する研究

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井　波　健　一

脾臓の内分泌学的性格の問題は脾臓の生理及び，病理に於て最も議論の多い問題である．このうち脾臓と骨髄に関する研究は少くないが，内分泌腺との相関に関する研究は遙かに少ない．著者は臨床的観察から脾臓と甲状腺の相関を想定し，臨床的並び実験的研究を行なつて之を立証した．

第一篇　脾腫患者の甲状腺のカテコールアミンによる急性一過性腫脹

1．褐色細胞腫患者の高血圧発作時，初期バセドウ氏病患者の精神興奮時などに急性一過性の甲状腺腫脹が観察されることがあるのは諸家の報告に見られるが，著者は2名の脾腫患者に Frey 氏試験のためカテコールアミンの注射を行なつた際に，同様の甲状腺の一過性腫脹が起るのを観察した．この現象は剔脾後には見られなくなり本現象と脾臓との関連を想定せしめた．そこで脾腫患者と対照にについて本現象を検討したところ，対照例に於ては1例も本現象が見られなかつたのに比し，脾腫患者13例中5例に於て本現象が観察され剔脾後には見られなくなつた．

2．生検によつて脾腫患者の甲状腺組織像を見ると著明な機能亢進又は低下の像は見られなかつたが全例に於て濾胞間毛細管の充盈が見られ対照との間に明らかな差異を認めた．甲状腺腫脹の観察された褐色細胞腫患者の甲状腺に於ても又濾胞間毛細管の充盈が見られることから，この充盈は甲状腺の急性腫脹の発現に意義を有するものと考えられる．

3．アルブミン感作法によつて家兎に実験的脾腫を作成するとその甲状腺にも同じく全例に濾胞間毛細管の充盈が見られた．しかもあらかじめ剔脾を行なつて感作した場合には充盈が見られないので本所見は脾腫に起因すると考えられる．

第二篇　甲状腺 I^{131} 摂取率に及ぼす脾臓の影響

家兎に於て脾臓の甲状腺機能に及ぼす影響を I^{131} 摂取率を用いて検討した．

1．剔脾後30日で摂取率は稍減少を示すが，50，150，270，410日では著明な亢進が見られた．

2．脾種作成の目的でアルブミン感作を行なつたが感作20日では摂取率は稍減少を示し，感作90日，即ち脾腫発現例では著明な亢進が見られた．しかるに脾腫剔除例及びあらかじめ脾剔を行なつて感作した例に於ても同様の亢進が見られ脾腫の影響は明らかではなかつた．

之等の事実は生理学的及び病理学的状態に於ける脾臓が甲状腺に諸種の影響を及ぼしていることを証明するものである．